IV. "On the Artificial Production of Fibrin from Albumen." By Alfred Hutchison Smee, Junior, Student of St. Bartholomew's Hospital. Communicated by W. S. Savory, Esq. Received January 15, 1863.

The condition in which fibrin exists in the blood and other fluids, and the deviation in quantity and quality in certain cases of disease from that of normal blood, has been to physiologists a subject of great interest. From the close resemblance of fibrin to albumen, I was induced to undertake a series of experiments, which appear to me to have some value in determining the conditions under which fibrin is derived from albumen, and which have resulted in the discovery of the general principle by which the direct conversion of albumen into fibrin may be effected. On referring to Lehmann's 'Chemistry,' in which the analyses of albumen and fibrin are quoted, it will be observed, on comparing them, that the difference appears to be the substitution of 1·5 part of oxygen per 100 for a similar amount of carbon, hydrogen, nitrogen, sulphur, phosphorus conjoined.

The following are the analyses quoted :—

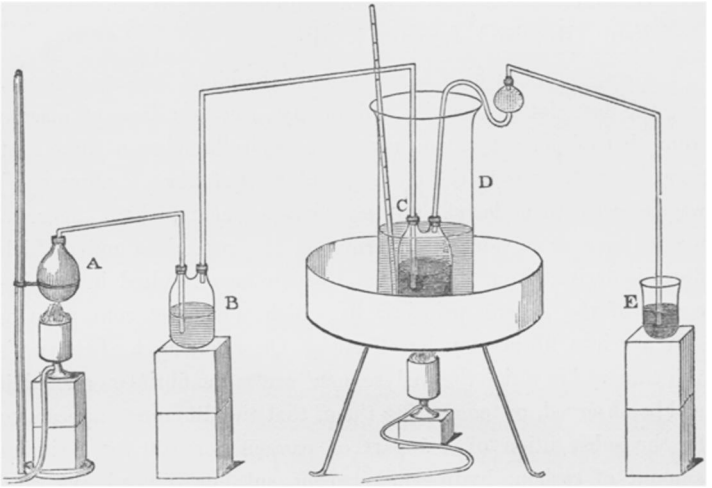
Albumen.		Fibrin.
53·5	Carbon	52·7
7·0	Hydrogen	6·9
15·5	Nitrogen	15·4
1·6	Sulphur	1·2
0·4	Phosphorus	0·3
22·0	Oxygen	23·5
100·0		100·0

The analyses made by Scherer give comparatively the same results.

From these analyses I was induced to make some experiments to endeavour to convert albumen into fibrin by the direct addition of oxygen gas, by which I anticipated that not only might the oxygen be imparted to the albumen, but also that the other elements might be oxidized and carried off.

In my first experiments I used blood from which the fibrin had been carefully whipped during the period of its coagulation, so that the serum might contain as many blood-cells as possible, upon the

supposition that the cells would afford a large amount of surface to the action of the gas.



The serum, after being whipped, was permitted to stand for twenty-four hours, that any fibrin which it might contain, and which had not coagulated during the process of whipping, might do so.

The apparatus used in all cases will be easily understood by referring to the annexed diagram. It consists, first, of a copper flask containing black oxide of manganese, from which the oxygen was slowly given off by the action of heat.

The gas was conveyed thence by tubes into a wash-bottle, B (containing a dilute solution of potass), for the absorption of impurities.

From the bottle B the gas passed into the flask C, which contained the defibrinated blood. This flask was placed in a vessel (D) containing water at a temperature varying between 95° and 100° Fahr.; and I had no difficulty in preserving that heat continuously by a small gas-flame placed under a sand-bath. After the gas had escaped from the blood, I generally passed it through a second portion of defibrinated blood contained in another vessel (E).

For all these experiments pig's blood was invariably chosen, on account of its richness in blood-cells.

My apparatus being ready, and oxygen being slowly given off, the whipped blood, from which every particle of fibrin had been previously removed, was introduced into the flask C.

The blood employed was arterial, and not venous. At first the bright scarlet colour of the blood increased somewhat, but after twelve hours the bright scarlet began to assume more the colour of venous blood: the cells at the same time began to shrivel. From this time the blood began rapidly to grow darker and darker, when, after thirty-six hours, it was almost black*.

Virchow has shown that, by acting on the hæmatin contained in the blood-cells by acetic acid, and subsequently boiling it, a substance is formed to which he gives the name of hæmine, which he considers to be a product in an intermediate stage between hæmatin and pigment. The black substance formed by oxidation may probably be found to be analogous to, if not identical with, Virchow's hæmin. I found in this blood, at the end of thirty-six hours, small masses, which had, under the microscope, the appearance of fibrin. A small portion of the same blood as that used in the experiment was set aside till the completion of the experiment, when it was examined, but no fibrin was found.

Likewise in the glass E, although the gas was passed through it without heat, no fibrin was found, proving that temperature had also an effect on the production of fibrin. This experiment was repeated many times: in all cases the blood assumed the black colour, but I did not invariably find fibrin.

The appearance of fibrin in some cases, and the non-appearance in many others, seemed at first sight to be inexplicable, though I shall be able to demonstrate, in a later portion of this paper, that the result may be explained upon the hypothesis that the alkaline salts were in relative excess in those cases where the fibrin did not appear.

In my next series of experiments, the white of an egg was added to about 4 oz. of the defibrinated blood. The egg-albumen at first had a tendency to separate and float at the top of the blood-serum, although well agitated together. In these cases the blood assumed the same dark colour as when it was subjected to experiment alone, though it did not appear until after the serum and egg-albumen had completely coalesced, which took place about ten hours after the subjection to temperatures between 95° and 100° Fahr., and the action of oxygen gas. At the end of thirty-six hours, the time when the experiment was stopped, masses of substances were found float-

* Crawford, about fifty years back, found that, after immersing animals in hot water, no difference could be discerned between arterial and venous blood.

ing, and also adhering to the bottom and sides of the vessel. These clots were in sufficient quantity to be collected and washed in the filter to free them from blood-cells and other impurities. The washed portion, under the microscope, had the distinct appearance of fibrin.

In cases where the albumen had not sufficient time to be mingled with the blood, little or no fibrin was formed. The time occupied for its absorption varied from about ten to twenty hours.

In the experiments which I conducted with albumen alone, I experienced at first some difficulty in obtaining the albumen perfectly pure, on account of the presence of chalazæ and other foreign matter. To obviate this difficulty, I found that, by adding one drop of glacial acetic acid to every white of egg employed, and then by well beating up the albumen, I obtained, on subsequent filtration, a clear solution which gave to litmus-paper a slightly acid reaction. On placing this transparent albumen in the ordinary apparatus, I found, after the passage of oxygen gas for four hours at the temperature before stated, that fibrin began to be formed. I found that, by placing coils of platinum wire in the albumen whilst undergoing oxidation, the formation of fibrin was not only greatly facilitated, but its subsequent separation from the rest of the albumen was accomplished with greater ease, as the fibrin hung in threads upon the platinum wire. When platinized platinum was used, the formation of fibrin, as might have been expected, was slightly improved.

Fibrin produced artificially in these experiments, and especially that formed on platinum wire, had a beautiful and regular arrangement, mostly being deposited in parallel lines. The fibrin likewise was whiter, and had a more delicate consistence than the common fibrin in blood.

I next tried the effect of adding a small quantity of a strong solution of ammonia to the albumen, which had naturally a slightly alkaline reaction; and then it was subjected to the influence of a current of oxygen in the same manner as in the preceding experiments. I found that fibrin was formed to a much smaller extent than when acid albumen was employed. The ammonia in all cases appears to be driven off to some extent by the oxygen, but was never entirely removed. The fibrin in this case formed on the surface of the liquid, and did not appear to be dissolved as the experiment was progressing.

It is worthy of particular observation, that fibrin was formed in the liquid which still contained ammonia in appreciable quantity.

My father suggested to me that it would be desirable to try the effect of the decomposition of water by electricity on albumen, as by that process the effect of hydrogen and oxygen in a nascent state is presented to different parts of the same fluid. For the purposes of this experiment I employed four cells (of the test-tube form) of Smee's battery, in which the negative pole consisted of a platinized platinum wire. This battery generated a continuous, but feeble, current of electricity; and the smallest perceptible bubbles were evolved from the platinized platinum wire when in operation for the experiment.

The albumen was placed in the decomposition trough, where a very large positive pole was employed, but a smaller negative one, and the temperature was maintained as in former experiments. After the passage of the electric current for some time, the positive pole of the decomposition cell was coated with a hard gelatinous mass, which, being immersed in water at 90° Fahr. for a few hours, unravelled itself into long fibres, which had, under the microscope, the appearance of fibrin.

On the negative pole, however, a frothy deposit alone was formed; but great care must be taken to stop the experiment before the products of the two poles grow together, to which they have a great tendency. The moment this takes place the albumen begins to coagulate, and in a very short time the whole becomes converted into an almost semisolid mass. The fibrin is not so perfect when made by this method, and is much more difficult to form than when made from neutral or slightly acid albumen by the ordinary process of oxidation.

In my experiments with egg-albumen to which a solution of potass had been added before it was subjected to the action of oxygen, the temperature ranging between 95° and 110° Fahr., no fibrin was found when the experiment was stopped.

In one case oxygen was passed through a solution of potass and albumen for three days and nights, and yet not the slightest trace of fibrin was found. The albumen became of a dark red hue, but two days after the experiment ceased it resumed its normal colour. A few transparent hard substances were found, insoluble in water and

weak acids which had separated from the albumen. A few other small white substances were noticed, which had all the appearance of carbonate of lime, and which were soluble in acid. Albumen was then mixed with gastric juice, and kept at the normal temperature of the body for the space of twelve hours, to produce artificial digestion, when it was subjected to experiment. I should here state that the gastric juice was procured from a dog, which had a fistulous opening made into its stomach by Professor Savory. All symptoms of inflammation and irritation had fully ceased; the dog, in fact, was in perfect health, and beginning to get fat, when the gastric juice was procured; so that the latter must be considered as healthy gastric juice. From the dog large quantities of gastric juice were obtainable; and I have to tender my best thanks to Professor Savory for his great kindness in placing whatever I required at my disposal. After the albumen had been digested for twelve hours and filtered, that the solution might be perfectly clear, it was subjected to the action of oxygen for a few hours, when fibrin was formed, though not in so large an amount as in albumen to which one drop of the glacial acetic acid had been added. The filaments of the fibrin, however, were of a more delicate constitution.

From a consideration of the above results, I thought that fibrin might be formed from the albumen which, after digestion with gastric juice, had passed through a membrane made of the parchment paper of Messrs. De la Rue and Gaines. In some experiments* to which I had been led from a study of Professor Graham's elegant researches on dialysis, and which I had formerly been conducting, on the passage of various fluids through membranes, it was observed that albumen, after digestion with gastric juice, dialysed to a certain extent. Three ounces of albumen were digested for the space of twelve hours, at the temperature of the body. It was then placed on the dialyser: it should be remarked that gastric juice does not coagulate the albumen during its conversion into albuminose.

The digested albumen was kept for ten hours on the dialyser at the temperature of 98° to 110° Fahr.

* These experiments, although carried on upon an extensive scale, are not quite in order for publication in detail; nevertheless I may state that, after artificial digestion, pure albumen, coagulated albumen, cheese, and, most remarkable of all, cod-liver oil were capable of passing through the dialyser into water to a large extent. I trust on a future occasion to elucidate this curious action.

The water (one and a half pint) into which the digested albumen had passed was concentrated at a temperature of not more than 80° Fahr.; and the concentrated solution being afterwards oxidized, I found that fibrin was formed, notwithstanding the changes it had undergone by digestion, which had rendered it capable of dialysis. During the process of passing oxygen into albumen, I found that carbonic acid was evolved. This was ascertained by passing the oxygen, after it had escaped from the albumen, through lime-water. I also found that phosphoric acid was evolved, by subjecting the effluent oxygen to the molybdate-of-ammonia test. Carbonic acid and phosphoric acid were also found when blood-serum was used, by the same tests as those employed when egg-albumen was the material used for experiment. In some cases common air was driven through albumen in the place of oxygen, at a temperature between 95° and 110° Fahr., and then I found the formation of fibrin differed but little from the quantity produced when oxygen alone was used. To ascertain whether the formation of fibrin was due really to oxygen alone, I tried hydrogen gas in the place of oxygen or common air, and at the same temperature. When hydrogen was passed into blood-cells sulphur was evolved. This was detected by passing the hydrogen, after it had traversed the serum, into a solution of lead-salt, and also by suspending over the serum strips of lead paper, when they soon became blackened by the sulphur.

When egg-albumen was employed instead of the blood-serum, sulphur was again detected.

Fibrin was not formed by the action of hydrogen on blood-serum or egg-albumen, although in some cases the hydrogen was passed continuously for forty-eight hours through the fluids. The action of carbonic acid gas on egg-albumen under the same condition of temperature produces no fibrin, but sulphur was again detected by suspending strips of lead paper over the albumen, which in a few hours became tinged.

The same result was obtained when defibrinated blood was used; but in this case, in addition to the sulphur, a minute trace of phosphoric acid was found. Not the slightest trace of fibrin was detected.

I conceived, from the result of my experiments on the oxidation of albumen, that, if oxygen was passed into milk, fibrin might be

formed, from the fact that the analyses of albumen of egg, and the casein which the milk contains, differ little from each other, and because the analysis of the milk of an animal, a few days before and after parturition, shows that albumen is found in the place of casein. On subjecting, however, milk to experiment, no fibrin was found after the lapse of twenty-four hours.

This may be due to either of two causes: first, the casein in the milk may not be in a fit state for undergoing the change before it has been acted on by the various digestive secretions, or, secondly, because in the dilute and fluid state in which it occurs in milk it does not offer sufficient resistance to the passage of the bubbles of oxygen to retain the gas sufficiently long for each bubble to have time to produce an effect. In all my experiments I have found (other conditions being equal) the slower the bubbles passed through the liquid material, and the more viscid the fluid was, the greater was the amount of fibrin produced. This may possibly in some degree account for the non-formation of fibrin when oxygen was passed through milk. I tried the effect of oxygen upon fresh grape-juice, but was unable to form any fibrin from it. Further experiments are required upon various vegetable juices.

I next experimented upon the oxidation of gluten, which was obtained from wheat-flour by the ordinary method. This was digested in gastric juice for twelve hours, and then filtered. After the clear liquid had been subjected to oxidation for some hours, small threads of a substance were formed. When a portion of this was placed under the microscope, no difference could be detected between it and ordinary fibrin.

From these experiments, it seems to me that the following conclusions may be drawn:—

First, that fibrin is produced by the direct action of oxygen on albumen.

Secondly, that the alkalies and alkaline salts prevent the appearance of fibrin when albumen is acted upon by oxygen.

Thirdly, that the formation of fibrin from albumen is accompanied by the evolution of sulphur, phosphorus, and carbonic acid.

Fourthly, That a temperature ranging between 98° and 110° Fahr. promotes the artificial formation of fibrin.

Fifthly, that the greatest amount of fibrin appears when the albumen is neutral or slightly acid.

Sixthly, that the viscidity of the material employed promotes the formation of fibrin.

Seventhly, that albumen, artificially digested in gastric juice, produces fibrin by its subsequent oxidation, even after dialysis.

Eighthly, that gluten dissolved in gastric juice, and then oxidized at the ordinary temperature, yields fibrin.

The formation of fibrin in the human body, and its relation to albumen, has long been a vexed question. I venture to put forward these experiments in connexion with this important and interesting inquiry.

V. "Note on the Spectrum of Thallium." By Professor William Allen Miller, M.D., LL.D., Treasurer and V.P.R.S. Received January 15, 1863.

My friend Mr. Crookes, the discoverer of the new metal thallium*, having kindly put into my hands a small quantity of the metal, which he believes to be chemically pure, I have been enabled to make some experiments upon its spectrum, the results of which may not be without interest to the members of the Royal Society.

Thallium, as is well known, when examined in the usual way by the spectroscope, yields a spectrum of remarkable simplicity, furnishing a single intense green line, the occurrence of which, as is familiar to chemists, led Mr. Crookes to the discovery of the metal, and suggested to him the name by which it is known. In order to try the effect of a progressively increasing temperature upon the spectrum furnished by the metal and its compounds, the following experiments were made.

* It has been made the subject of question abroad, whether Mr. Crookes or M. Lamy was the first to recognize the metallic nature of thallium, and thus to dispute the claim of Mr. Crookes to the full credit due to him for his investigation (with only about twenty grains of the element) of its leading characters where no previous clue existed to guide him. It may be sufficient to state in answer to this suggestion, that Mr. Crookes had exhibited it at the International Exhibition, and marked as *metallic* his scanty store, though in the form of a precipitate, in the beginning of May, unquestionably before M. Lamy had published anything relating to thallium.